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EXAMINER	
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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 18

Application Number: 09/353,407
Filing Date: 07/15/99
Appellant(s): Lubenow et al.

Thomas Berka
For Appellant

EXAMINER'S ANSWER

This is in response to appellant's brief on appeal filed on July 20, 2001.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

Appellant's brief includes a statement that Jepson format claims 2, 34, 64 and 66 do not stand or fall together with other independent claims 1 and 33 and provides reasons as set forth in 37 CAR 1.192(c)(7) and (c)(8).

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

The following is a listing of the prior art of record relied upon in the rejection of claims under appeal.

5,942,391	Zhang	8-1999
5,466,577	Weisburg	11-1995
5,646,016	McCoy	7-1997
5,798,442	Gallant	8-1998
4,009,213	Stein	2-1977

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1-66 are rejected under 35 U.S.C. 102 and 103. This rejection is set forth in prior Office action, Paper No. 10, and set forth below.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

2. Claims 1-4, 9, 13-18, 19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 are rejected under 35 U.S.C. 102 (e) as anticipated by Zhang et al. (U.S. Patent 5,942,391) (August 24, 1999).

Zhang et al teaches a method for isolating a molecule from a sample in a vessel (Example 1 and Example 9), comprising the steps of :

a) providing a multiplicity of magnetic affinity particles and incubating the particles in the presence of a detergent (Example 1, Column 27, lines 31-40, Example 9, column 39, line 56 to column 40, line 4);

b) combining the sample containing a molecule of interest with the affinity particles suitable for binding the molecule, the affinity particles being insoluble in the sample (Example 1, Column 27, lines 31-40, Example 9, column 39, line 56 to column 40, line 4);

c) immobilizing the magnetic affinity particles by applying a magnet to the vessel (Example 1, column 27, lines 42-46 and Example 9, column 40, lines 9-12);

d) separating the remainder of the sample from the immobilized magnetic affinity particles (Example 1, column 27, lines 45-46 and Example 9, column 40, lines 11-12);

e) optionally, resuspending the affinity particles in a solution (Example 1, column 27, lines 50-52 and Example 9, column 40, lines 12-18);

f) optionally, eluting the molecules from the affinity particles, followed by separating the affinity particles from the eluted molecules (Example 1, column 27, line 52 to column 28, line 29 and Example 9, column 40, lines 19-39);

wherein any of the steps b), c) ,d), e) if present, and f) if present may optionally be also performed in the presence of the detergent, wherein the use of detergent is sufficient to reduce loss of particles during any separation step (Example 1, column 27, line 52 to column 28, line 29 and Example 9, column 40, lines 19-39).

Zhang et al teaches a method wherein the combining step (a) is carried out in the absence of detergent, but detergent is added prior to the separation step (b) (Example 9, column 40, line 6).

Zhang et al teaches a method wherein the molecule of interest is selected from nucleic acids (Examples 1 and 9).

Zhang et al teaches a method wherein the particles are selected from streptavidin-coated superparamagnetic beads (Example 1, column 27, lines 37-38 to column 28, line 29 and Example 9, column 40, lines 1-2).

Zhang et al teaches a method wherein the particles are composed of materials selected from Aluminum silicates (Example 9, Column 40, line 1).

Zhang et al teaches a method wherein the nonionic detergent P-40 , a polyoxyethylene sorbitol monolaurate, is at a concentration of from about 0.0005% to 2.0% (v/v) (Example 9, column 39, line 59 and column 40, line 6).

3. Claims 1-4,9, 13-17, 20, 33-35, 44-46,48, 49 and 64-66 are rejected under 35 U.S.C. 102 (b) as anticipated by Weisburg (U.S. Patent 5,466,577) (November 14, 1995).

Weisburg teaches a method for isolating a molecule from a sample in a vessel (Example 3), comprising the steps of :

a) providing a multiplicity of magnetic affinity particles and incubating the particles in the presence of an anionic detergent SDS (Example 3, column 8, lines 1-6);

b) combining the sample containing a molecule of interest with the affinity particles suitable for binding the molecule, the affinity particles being insoluble in the sample (Example 3, column 8, lines 10-15);

c) immobilizing the magnetic affinity particles by applying a magnet to the vessel (Example 3, column 8, lines 15-19);

d) separating the remainder of the sample from the immobilized magnetic affinity particles (Example 3, column 8, lines 15-19);

e) optionally, resuspending the affinity particles in a solution (Example 3, column 8, lines 20-23);

f) optionally, eluting the molecules from the affinity particles, followed by separating the affinity particles from the eluted molecules (Example 3, column 8, lines 20-23);

wherein any of the steps b), c) ,d), e) if present, and f) if present may optionally be also performed in the presence of the detergent, wherein the use of detergent is sufficient to reduce loss of particles during any separation step (Example 3).

Weisburg teaches a method wherein the combining step (a) is carried out in the absence of detergent, but detergent is added prior to the separation step (b) (Example 3).

Weisburg teaches a method wherein the molecule of interest is selected from nucleic acids (Example 3, column 8, lines 1-2).

Weisburg teaches a method wherein the particles are selected from oligo-thymidine coated magnetic beads (Example 3, column 8, lines 10-12).

Weisburg inherently teaches a method wherein the particles are composed of materials selected from metal oxides (Example 3, column 8, lines 10-12).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-4,9, 13-17, 20, 25, 26, 33-35, 44-47,48, 49 , 56 , 57 and 64-66 are rejected under 35 U.S.C. 103 (a) in view of Weisburg (U.S. Patent 5,466,577) (November 14, 1995).

Weisburg teaches the method of claims 1-4,13-17, 20, 33-35, 44-46,48, 49 and 64-66 as described above.

Weisburg does not specify the concentration of anionic detergent in the range of .0005% to 2%.

However, it is *prima facie* obvious that selection of the specific concentration of a known detergent represents routine optimization with regard to production of desired soluble components which routine optimization parameters are explicitly recognized to an ordinary practitioner in the relevant art. As noted *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the specific concentration selection performed was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

7. Claims 1-18, 19, 23, 24, 31-50, 54, 55 and 62-66 are rejected under 35 U.S.C. 103 (a) over Zhang et al. (U.S. Patent 5,942,391) (August 24, 1999) in view of McCoy et al (U.S. Patent 5,646,016) (July 8, 1997).

Zhang et al teaches the method of claims 1-4,9, 13-18, 19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 as described above.

Zhang et al does not teach a method wherein the molecule is a protein fused to metal chelating group containing six consecutive histidine residues.

McCoy et al teaches a method wherein the molecule is a protein fused to metal chelating group containing six consecutive histidine residues (Example 16, column 29, lines33-60 and column 3, line 34 to column 4, line 9).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the affinity purification using histidine patch containing fusion proteins of McCoy et al in the affinity purification method of Zhang et al since McCoy et al states, "However, the present invention provides, inter alia, the modification of a fusion partner protein, e.g., thioredoxin., in such a way as to enable it to bind to a metal chelate affinity matrix, providing an additional convenient purification tool that can be used for fusion proteins. The technique is also applicable to other proteins, including other fusion partner proteins, and proteins which are not fusion protein constructs (column 3, lines 24-31)". McCoy et al. further provides motivation as he states, "There is provided another novel method for increasing the production of soluble recombinant proteins (column 4, lines 22-24)". An ordinary artisan would have been motivated by the express statement of McCoy to utilize the histidine patch containing fusion proteins of McCoy et al in the method of Zhang et al in order to achieve the express advantage of an improved affinity purification method with an additional convenient purification tool ,as noted by McCoy et al, which can be used for increasing the production of soluble recombinant proteins and satisfactorily purifying them..

8. Claims 1-4, 9, 13- 19, 21, 23, 29-35, 44-50,52, 54, 55 and 60-66 are rejected under 35 U.S.C. 103 (a) over Zhang et al. (U.S. Patent 5,942,391) (August 24, 1999) in view of Gallant

et al (U.S. Patent 5,798,442) (August 25, 1998).

Zhang et al teaches the method of claims 1-4, 9, 13-18, 19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 as described above.

Zhang et al does not teach the use of zwitterionic detergent 3-[cholamido-propyl)-dimethyl-ammonio]-1-propanesulfonate.

Gallant et al teaches the use of zwitterionic detergent 3-[cholamido-propyl)-dimethyl-ammonio]-1-propanesulfonate in affinity purification method (Column 22, lines 33 to column 23, line 27).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the affinity purification method with suitable zwitterionic detergent of Gallant et al in the method of Zhang et al in order to separate any protein or nucleic acid from any biological sample. An ordinary artisan would have been motivated to utilize the equivalent chaotropic agents along with the affinity purification method of Gallant et al in the affinity purification method of Zhang et al in order to accomplish the considerable and satisfactory purification of proteins and nucleic acids with useful chaotropic agents.

9. Claims 1-4, 9, 13-19, 22, 27- 29, 31-35, 44-50, 52, 53- 55 and 58-66 are rejected under 35 U.S.C. 103 (a) over Zhang et al. (U.S. Patent 5,942,391) (August 24, 1999) in view of Stein et al (U.S. Patent 4,009,213) (February 22, 1977).

Zhang et al teaches the method of claims 1-4, 9, 13-18, 19, 23, 24, 31-35, 44-50, 54, 55 and 62-66 as described above.

Zhang et al does not teach the use of cationic detergent dodecyl trimethyl ammonium chloride.

Stein et al. teaches the use of cationic detergent dodecyl trimethyl ammonium chloride. (Example 8, column 17, lines 65-67).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the suitable cationic detergent of Stein et al in the method of Zhang et al since Stein et al states, "The use of the cationic compounds is preferred in the separation of fatty alcohols of different melting points (column 6, lines 22-24)". An ordinary artisan would have been motivated by the express statement of Stein et al. to utilize the cationic detergents of Stein et al in the method of Zhang et al in order to achieve the express advantage of a method ,as noted by Stein et al, which can be preferably used for accomplishing separation of fatty alcohols of different melting points.

(11) Response to Argument

Appellant agrees that both Zhang and Weisburg references teach exactly the same structure and chemical composition of the claimed invention and may have enjoyed the benefit of practicing Appellants' claimed invention (Page 17 of the Appeal Brief) but the Appellant argues that the references are silent about the problem and benefit of the claimed invention. Appellant argued that none of the references teach or suggest the problem of affinity particle loss during affinity separation procedure and the benefit of contacting affinity particles with detergent prior to the step of manipulating the particles to reduce particle loss compared to the affinity procedures in the absence of the detergent. Appellant cites *In re Zierden* for the proposition that a new use of a known process is patentable and that accidental use cannot anticipate the claimed invention. However, *In re Zierden* is not the final word in case law on this subject. In an old decision, the CCPA *In re Woodruff,* noted (1) "it is a general rule that merely discovering and claiming a new benefit of an old process cannot render the process again patentable. While the process encompassed by the claims are not entirely old, the rule is applicable here to the extent that the claims and the prior art overlap" See *In re Woodruff,* 16 U.S.P.Q. 2d (CCPA 1934). (2) Another decision by the 5th circuit Board recites,"When the process has been in well-established use, however, novelty is destroyed even though some of the benefits of the process are not recognized or appreciated", See *Bird Provision Co. V. Owens Country Sausage, Inc.* 197 U.S.P.Q. (CCPA 134).

Finally two recent CAFC case laws make it clear,"Where, as here, the result is a

necessary consequence of what was deliberately intended, it is of no import that the article's authors did not appreciate the results", See *MEHL/BIOPHILE V. Milgraum,* 192 F.3d 1362, (CAFC 1999). "Newly discovered results of known processes directed to the same purpose are not patentable because such results are inherent", See *Bristol-Myers Squibb V. Ben Venue Laboratories,* Inc., 246 F. 3d 1368, (CAFC 2001).

Now in applying this case law, the role of *Bristol-Myers Squibb V. Ben Venue Laboratories,* is to distinguish between two situations, the new use situation and the situation of a newly described result of an old process. In the current case, as can be seen in the field of invention, "The present invention provides a method for isolation and assay of molecules of interest using affinity matrices in the presence of detergent" (Page 1, lines 15-16 of the Specification). The specification further notes, "In its broadest aspects, the present invention relates to a method of separating particles from a solution comprising the steps: a) combining a solution with a finely divided particulate matrix, in the presence of a detergent; b) collecting the particles of the particulate matrix, e.g., by centrifugation, filtration, magnetic force (if the particles are magnetically attractable), etc; c) removing supernatant solution." (Page 4, lines 12-18 of the Specification). This broad invention is an old process, which is expressly taught by both Zhang and Weisburg references, what Appellant claims is the new use in the appeal brief. Appellant describes an unexpected result in the specification, as the specification notes, "Unexpectedly, it has now been shown that the use of small amounts of detergents in conjunction with the use of affinity beads, the loss of beads can be significantly reduced (Page 3, lines 24-

26)". From the case law, it is clear that an inherent result, however unexpressed, is simply a newly discovered result of an old process, whereas the purpose of Zhang as well as Weisburg is the same as Appellant i.e. to purify a target molecule using an affinity column. In conclusion, this inherent result is not patentable over the old process described in the prior art.

Further, if the Zhang or Weisburg method were performed after the issuance of a patent to the current Appellant, it is absolutely clear that such a performance would literally infringe such a patent. In that hypothetical litigation, neither Appellant nor the court would accept the reasoning of the hypothetical infringer that they had not intended to infringe. If the hypothetical infringer had performed the exact same method steps, intending to perform an affinity isolation procedure such as that of Zhang or the specification, but had not intended to achieve the new use of reduction of loss of affinity particles, the hypothetical infringer would found to literally infringe the Appellant's hypothetical patent. As the court notes in Bristol Myers, " it is axiomatic that which would literally infringe if later anticipates if earlier". Therefore, it is clear that the current prior art functions to properly anticipate and render obvious the claimed invention, since the cited prior art would literally infringe the claims.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant also argues that there is no motivation to combine Zhang reference with McCoy, Gallant or Stein references. This

argument is not persuasive in presence of the express motivations mentioned as follows: McCoy et al states, "However, the present invention provides, inter alia, the modification of a fusion partner protein, e.g., thioredoxin., in such a way as to enable it to bind to a metal chelate affinity matrix, providing an additional convenient purification tool that can be used for fusion proteins. The technique is also applicable to other proteins, including other fusion partner proteins, and proteins which are not fusion protein constructs (column 3, lines 24-31)". Moreover, Stein et al states, "The use of the cationic compounds is preferred in the separation of fatty alcohols of different melting points (column 6, lines 22-24)".

Applicant also argues that HPLC column method of Gallant reference is not applicable to affinity particles method of the claimed invention because it lacks some manipulative procedures of affinity particles e.g., collecting the affinity particles, separating the affinity particles with bound molecules by washing and eluting. This argument is not persuasive. An ordinary artisan with a skill in the art of biomolecule purification would have obviously practiced and substituted the manipulative procedures of affinity particles of claimed invention which are well known and routinely practiced in the art in the method of Gallant et al to achieve reasonable amount of success.

In summary, as the purposes of the prior arts and the current invention are similar, an inherent, newly discovered result carries no further patentable weight.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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August 2, 2001

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